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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,452		Masayuki Yabuta	58777.000008	5707

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EXAMINER	
ROOKE, AGNES BEATA	
ART UNIT	**PAPER NUMBER**
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/030,452	YABUTA ET AL.	
	Examiner	Art Unit	
	Agnes B. Rooke	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3-6,8-10,14,17,18 and 21-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3-6,8-10,14,17,18 and 21-36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This NON-FINAL office action is in response to the paper filed on 6/26/2007. The amendments to the claims are acknowledged. New claims 21-36 have been added.

Status of Claims

Claims 1, 2, 7, 11-13, 15, 16, 19, and 20 are cancelled.

Claims 3-6, 8-10, 14, 17, 18, and 21-36 are pending and under consideration.

Priority

The Applicants claim priority to JAPAN 2000-137228, filed on 05/10/2000, is acknowledged.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 3-6, 8-10, 14, 17, 18, and 21-36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In the independent claims 9, 10, 17, 18, 33, and 35, the word "byproduct polypeptide" is indefinite since examiner cannot estimate metes and bounds of the claim, since the byproduct peptide is not defined and no examples are provided in the claims. All independent claims are included in this rejection because they do not cure the deficiencies of the independent claims by further defining the byproduct polypeptide.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 3-6, 8-10, 17, 18, and 21-31, 33, and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Hobden et al., UK Patent Application GB 2180539,(published on April 1, 1987).

Hobden et al. teach a hybrid protein comprising a first polypeptide having human ANF. See Abstract; where the DNA mixture derived was used to transform E.coli JM103. See page 10, line 26; where the overnight culture of E.coli JM103 was diluted a hundred-fold into fresh L-broth (30 ml comprises tryptone, yeast extract and NaCl; See page 10, lines 27-28; where the yeast extract is composed of different amino acids (See "Manual of BBL Products and Laboratory Procedures, pages 293-294, please refer to the copy as it was attached to the previous office action).

Applicants stated that examiner did not present any evidence in the prior art cited that would supported an inherency argument that all limitations of the rejected claims are present in Hobden reference support by the Manual of Laboratory Procedure.

Examiner maintains the rejection and applies the inherency argument because L-broth contains yeast extract and thus will contain amino acids such as methionine, histidine, or glycine. Examiner cited the manual for laboratory procedures to show that it is understood in the prior art that the amino acids of interest are present in the L-broth formulation and thus Hobden et al. still applies.

Claims 3-6, 8-10, 17, 18, and 21-31, 33, and 35 are rejected under 35 U.S.C. 102(e) as being anticipated by Ueda et al. (U.S. 2003/0170811 A1).

Ueda et al. teach a process for the production of alpha-human atrial natriuretic polypeptide by recombinant technology. See Abstract.

On page 9, paragraph [0112] teaches expression of a gene coding for the peptide Cla-Fused alpha-hANP (ClaH Protein); where an overnight culture of E.coli H1 containing the expression vector, plasmid pCLaHtrpSd in L-broth, where the E.coli was cultured [0113]; where the L-broth according to the "Handbook of Microbiological Media," (see page 725, as the copy was attached to the previous office action) contains yeast extract, which is composed of different amino acids.

Applicants state that examiner did not support the rejection by inherency since the handbook of microbiological media as cited in the last office action does not specifically point out the amounts of amino acids that are included in the L-broth.

Examiner responds that L-broth with the yeast extract is commonly used in the art as a source of amino acids and thus the reference of Ueda et al. still applies.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 3-6, 8-10, 14, 17, 18, and 21-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yabuta et al. (U.S. 5,670,340).

Yabuta et al. teach a process of expression a target peptide in a large amount and accumulation of the target peptide in host cells in the form of occlusion bodies. See Abstract. In Examples 3 and 4, Yabuta et al. teach production of human calcitonin from fusion protein in E.coli. Examples 5-8 teach production of CNP-22 from fusion protein in E.coli. In column 13, line10, Yabuta et al., teach addition of 2.0 g/L of L-methionine to the culture medium. In column 4, lines 30-32, the preferable host is Escherichia coli.

Yabuta et al. do not teach production of ANP from fusion protein in E.coli.

In column 4, line 20-26, Yabuta et al. state that the method can be applied for production of a fusion protein of physiologically active peptides, for example natriuretic peptides, such as ANP. In Claim 1, Yabuta et al. claim process for the production of a target peptide, where the target peptide can be ANP.

It would have been obvious to a person of ordinary skill in the art to substitute ANP for human calcitonin or CNP as per teachings of Yabuta et al. because the same result should be expected when using ANP in place of CNP or clacitonin. It would be predictable that the method would work with ANP because Yabuta et al. showed that

the method was successful with calcitonin and CNP, because Yabuta et al. stated that the same method would work for ANP.

Further, claims 13 and 14 are included in this rejection because in the absence of the evidence to the contrary, the addition of 3.0 g/L of L-methionine as claimed, instead of 2.0 g/L of L-methionine as taught by Yabuta et al. would not make a significant difference in the outcome of reducing formation of a byproduct polypeptide comprising O-acetylserine residue in place of serine.

One skilled in the art would be motivated to use ANP in place of calcitonin or CNP because the steps in the method disclosed by Yabuta et al. would be the same, and the expectation of success would be high because of the great results achieved by Yabuta et al. Further, an addition of 3 g/L of L-methionione, instead of 2.0 g/L of L-methionine as taught by Yabuta et al. would be strongly desirable, since the effects of using 2.0 g/L were successful.

In addition, in the pending claims, the Applicant claims O-acetylserine as a byproduct formed in the method of production of an atrial natriuretic peptide comprising a serine residue.

MPEP section 2106 states that language that suggests or makes optional, but does not require steps to be performed or does not limit a claim to a particular structure, does not limit the scope of a claim or claim limitation. For example, a language that may raise a question as to the limiting effect of the language in a claim are statements of intended use or field of use. Therefore, the byproduct O-acetylserine has no effect on

the steps performed in the method, therefore O-acetylserine does not limit the claims as currently presented.

Therefore, it would have been obvious to one skilled in the art to design a method for the production of a protein comprising culturing E.coli host cells transformed with a plasmid capable of expressing the protein, where the protein produced is the human atrial natriuretic peptide as suggested by Yabuta et al., and where the byproduct formed is in a form of O-acetyl-serine. One would be motivated to produce the atrial natriuretic peptides because of the success of the method in producing a human calcitonin as taught by Yabuta et al.

Applicants responded that Yabuta et al. do not teach limitations that refer to a step of adding methionine and at least one of histidine or glycine to the medium in an amount effective to reduce byproduct formation and that the formation of byproduct polypeptide is reduced in an amount greater than or equal to 50% when compared to a control medium with no methionione, histidine, or glycine added and that 3 g/L of methionine is used in the method.

Examiner respectfully states that the production of O-acetyl-serine as a byproduct would be expected as part of a cysteine metabolic pathway in E.coli during the production of a protein comprising culturing E. coli host cells transformed with a plasmid capable of expressing the protein where the protein produced is a human ANP, as suggested by Yabuta et al. In addition, it is pointed out on page 17 of the specification, lines 21-26, that any one of amino acids: alanine, glycine, serine,

methionine or histidine can be added to the suspension of the cell culture in the instant invention, and that Yabuta et al. teach addition of L-methionine, for example. Also, the byproduct will be reduced when compared to a medium with no methionine. Further, Yabuta et al. teach addition of 2.0 g/L of L-methionine, however in the absence of the evidence to the contrary it will be still obvious to add 3 g/L of methionine to achieve the same goal.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Agnes Rooke whose telephone number is 571-272-2055. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-272-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197.

AR

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PRIMARY EXAMINER